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EXAMINER
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HENLEY III, RAYMOND J

ART UNIT	PAPER NUMBER
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1614

DATE MAILED: 07/24/2003

7

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/024,040

Applicant(s)

GARVEY ET AL.

Examiner

Raymond J. Henley III

Art Unit

1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE \_\_\_\_\_ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on 01 July 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 8-12 is/are pending in the application.
- 4a) Of the above claim(s) 8 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) 9 and 10 is/are rejected.
- 7) ☐ Claim(s) 11 and 12 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_ 6) ☐ Other: \_\_\_\_\_

**CLAIMS 8-12 ARE PRESENTED FOR EXAMINATION**

Applicants' Abstract filed April 9, 2002, Preliminary Amendment filed December 21, 2002 and Response filed July 1, 2003 have been received and entered into the application.

Accordingly, the Abstract has been added; claims 1-7 have been canceled; claims 8-12 have been added; and the specification at page 1 has been amended.

In Applicants' most recent response, Applicants' election, without traverse, of group II, claims 9 and 10 is acknowledged. The Invention of group II also includes newly added claims 11-12. Having made the election without traverse, the restriction requirement set forth in the previous Office action dated June 9, 2003 is deemed to remain proper and herein made FINAL.

***Clarification/Further Information Requested***

In applicant's most recent response, at the amendment to the specification at page 1, it is set forth that the present application merely "claims priority" to U.S. Application No. 09/354,424. It is requested that applicant provides the nature of the priority under 35 U.S.C. 120 and/or 121.

Also, at the same section of the amendment, it is set forth that U.S. Application No. 09/354,424 is a continuation of U.S. Application No. 09/354,424. The designation as a continuation is inconsistent with Office records which show that the two applications are related as divisionals. Clarification is requested.

***Claim Rejection - 35 USC § 112, First Paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to

Art Unit: 1614

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

***I      Written Description***

Claims 9-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams and formula that fully set for the claimed invention. *Lockwood v. American Airlines, Inc.*, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

Claim 9 contains a listing of nitrovasodilators selected from the group consisting of sodium nitroprusside, diazenium diolates, molsidomine, linsidomine chlorohydrate, S-nitrosothiols, organic nitrates, pharmacologically acceptable salts, esters, analogs, derivatives, prodrugs and inclusion complexes of any of the foregoing and combinations thereof.

In the response filed July 1, 2003, applicants have pointed to page 4, line 28 to page 5, line 1; page 7, lines 9-17; page 56, line 6 to page 57, line 21 as being supportive of the invention as claimed. Page 4, line 28 to page 5, line 1 provides support for the treatment of female sexual dysfunction employing vasodilators. Page 7, lines 9-17 provides for the concept of the treatment of female sexual dysfunction in which a compound is administered which is a PDE inhibitor which can optionally be substituted with at least one NO or NO<sub>2</sub> moiety and a compound that donates, transfers or releases nitric oxide as a charged species, i.e., nitrosonium, nitroxyl or as nitric oxide. Page 56, line 6 to page 57, line 21 sets forth further types of NO adducts and nitrosylated compounds.

Art Unit: 1614

The present specification, does not however, describe the presently claimed compounds, *with the exception of S-nitrosothiol compounds*, using such descriptive means as words, structures, figures, diagrams and formula that fully set for the claimed invention concept. Nothing in the present specification would lead one to select “organic nitrates” as a whole. Also, nothing in the specification would lead one to conclude that the concept of the specific compounds sodium nitroprusside, i.e., Ferrate(2-), pentakis(cyano-C)nitrosyl-; a diazenium diolate compound, e.g., Diethylamine diazeniumdiolate which is Ethanamine; Molsidomine, i.e., 2,2'-(hydroxynitrosohydrazono)bis- 1,2,3-Oxadiazolium, 5-[(ethoxycarbonyl)amino]-3-(4-morpholinyl)-, inner salt; Linsidomine chlorhydrate, i.e. 3-Morpholinosydnone imine monohydrochloride.

Further, in claim 9 (and thus claim 11), it is recited that the composition is administered “to the vagina, vulvar area and/or urethra of the individual” and claim 8 (and thus claim 12) recites “administering to a surface of the clitoris” as a means for administration. In the present specification, the Examiner can only locate the following teachings that relate to administration of the disclosed compounds for the purpose of treating female sexual dysfunction:

“In another aspect, the invention provides a method for treating female sexual dysfunction in humans which comprises administering to an individual in need thereof a therapeutically effective amount of a nitrosated or nitrosylated PDE inhibitor.” [page 7, second paragraph]

”The nitrosated or nitrosylated PDE inhibitor and the compound that donates, transfers or releases nitric oxide and/or stimulates endogenous production of NO or EDRF in vivo can be administered separately or as components of the same composition in one or more pharmaceutically acceptable carriers.” [page 8, first paragraph]

”When administered in vivo, the nitric oxide may be administered in combination with pharmaceutical carriers and in dosages described herein.” [page 59, fourth full paragraph]

“The nitrosated or nitrosylated compounds of the invention are used at dose ranges and over a course of dose regimen and are administered in the same

Art Unit: 1614

or substantially equivalent vehicles/carrier by the same or substantially equivalent oral or nasal inhalant devices as their non-nitrosated or non-nitrosylated counterparts. The nitrosated or nitrosylated compounds of the invention can also be used in lower doses and in less extensive regimens of treatment. The amount of active ingredient that may be combined with the carrier materials to produce a single dosage form will vary depending upon the host treated and the particular mode of administration.” [page 59, last paragraph]

Also, page 60 relates to the administration of the disclosed compounds and reads, in its entirety:

“The dosage regimen for treating a disease condition with the compounds and/or compositions of this invention is selected in accordance with a variety of factors, including the type, age, weight, sex, diet and medical condition of the patient, the severity of the disease, the route of administration, pharmacological considerations such as the activity, efficacy, pharmacokinetic and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered as part of a drug combination. Thus, the dosage regimen actually employed may vary widely and therefore may deviate from the preferred dosage regimen set forth above.

Total daily dose administered to a host in single or divided doses may be in amounts, for example, from about 1 to about 100 mg/kg body weight daily and more usually about 3 to 30 mg/kg. Dosage unit compositions may contain such amounts of submultiples thereof to make up the daily dose.

While the compounds of the invention can be administered as the sole active pharmaceutical agent, they can also be used in combination with one or more compounds which are known to be effective against the specific disease state targeted for treatment. The compositions of the invention can also be administered as described above or can be made to include one or more additional active compounds which are known to be effective against the specific disease state is targeted for treatment.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.”

Considering the teachings provided by applicants, the Examiner believes that applicant has failed to provide a the necessary teaching , by describing the claimed invention with all of

Art Unit: 1614

its limitations using such descriptive means as words, structures, figures, diagrams and formula that fully set for the claimed invention, in such a way as to reasonably convey to one skilled in the relevant art that the disclosed compounds could or should be administered in the manner presented in the claims.

Accordingly, the Examiner finds that claim 46 is properly rejected.

## ***II      Enablement***

Claims 9-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The above text set forth by the Examiner under the "Description" heading is herein incorporated by reference.

As set established in the above rejection, the compounds of claim 9, *with the exception of S-nitrosothiol compounds*, and the means of administration of claims 9-12 are not described in the present specification. It would logically follow that such a limitations would then necessarily not be described in such a way to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention as claimed.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

When the above factors as applied to the present application (see below) are weighed, it is the examiner's position that the present specification would not enable the skilled artisan to use

Art Unit: 1614

the presently claimed compounds of claim 9, *with the exception of S-nitrosothiol compounds*, or to administer any of the disclosed compounds in the manner required by either claim 8 or 9 because applicants have not disclosed or described that the presently claimed compounds, *with the exception of S-nitrosothiol compounds*, may be used or that the compounds may be administered “to the vagina, vulvar area and/or urethra of the individual” (claim 9) and “administering to a surface of the clitoris” (claim 8).

(1) The nature of the invention.

The presently claimed invention is directed to the treatment of female sexual dysfunction (claim 9) or enhancing sexuality in a female having a clitoris (claim 9). To achieve such objectives vasodilators are administered “to the vagina, vulvar area and/or urethra of the individual” (claim 9) and “administering to a surface of the clitoris” (claim 8).

(2) The state of the prior art.

Claim 1 of U.S. Patent No. 6,306,841, which claims domestic priority to October 28, 1997, is duplicated by applicants as claim 9, thus the art was aware of that claimed subject matter.

The prior art also recognized methods for modulating the excitation and plateau phases of the female sexual response on demand by transmucosal, transdermal, intranasal, or rectal administration of an effective amount of vasodilator agent. See U.S. Patent No. 5,565,466 (Gioco et al.) at column 4, lines 10-15.

(3) The relative skill of those in the art.

The relative skill of the those in the art is high.

(4) The predictability or unpredictability of the art.

Art Unit: 1614

Due to the idiosyncratic nature of humans or other animals, drug response in one subject does not always equate to the same response in another subject. The unpredictability of the pharmaceutical chemistry art is very high.

(5) Breadth of the claims.

Claim 9 (dependent claim 11 is directed to a specific vasodilator compound) is directed to treating sexual dysfunction in a female individual by specific means of administration using specific vasodilator compounds. Claim 8 (dependent claim 12 is directed to a specific vasodilator compound) is specifically directed to a method for enhancing sexuality in a female having a clitoris through the topical administration of a vasodilator composition.

(6) The amount of direction or guidance presented.

As outlined above under the heading "Written Description", applicants have failed to disclose a basis for selecting the specifically claimed compounds of claim 9, *with the exception of S-nitrosothiol compounds*, or for administering the compounds in the manner specified in the claims. The Examiner's position based upon such a finding is not inadequate direction or guidance is present to practice the invention as claimed in present claims 8-12.

(7) The presence or absence of working examples.

At page 66, Example 3, applicants have provided an *in vitro* comparative study on relaxation responses in human corpus cavernosum tissue wherein dipyridamole or a compound of the present invention was employed. No working examples are present which are reflective of the subject matter of claims 8-12.

(8) The quantity of experimentation necessary.

Because of the unpredictability of the art, see (4) above, and that applicants' disclosure fails to provide a written description of the specifically claimed compounds, *with the exception*

*of S-nitrosothiol compounds*, and the presently claimed means for administration, it is believed that undue experimentation would be necessary to practice the invention claimed.

Accordingly, claims 8-12 are deemed to be properly rejected under 35 U.S.C. 112, first paragraph.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 9 and 11 are rejected under 35 U.S.C. 102(a) as being anticipated by Place et al. (U.S. Patent No. 6,306,841). See claim 1 and line 7 thereof where “S-nitrosothiols” is set forth which corresponds to present claim 11.

***Applicants’ Request for Interference***

While applicants have copied claim 1 of Place et al. in order to provoke an interference, Place et al. has an earlier effective filing date than applicants, i.e., October 28, 1997 for Place et al. vs. October 31, 1997 for applicants. Accordingly, Place et al. is prior art and an interference cannot be provoked therewith (MPEP 2306) in the absence of a declaration under 37 CFR 1.608.

Also, applicants have copied claim 1 of Wysor et al. for the purpose of provoking an interference. An interference cannot be provoked therewith because at least one claim must be patentable to applicants in order to provoke an interference (MPEP 2306) and such is not the case here where all of applicants’ claims have been rejected under 35 USC § 112, First Paragraph.


Art Unit: 1614

Accordingly, for the above reasons, claims 8-12 are deemed to be properly rejected and none are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Raymond J. Henley III whose telephone number is 703-308-4652. The examiner can normally be reached on Flex.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel can be reached on 703-308-4725. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

  
Raymond J. Henley III  
Primary Examiner  
Art Unit 1614

rjh  
July 14, 2003